

WHAT IS CLAIMED IS:

1. A method for treating a vascular disease in a mammal, wherein said method comprising the steps of:

infected a segment of a blood vessel *in vitro* using a gutless adenoviral vector comprising a polynucleotide encoding a thrombomodulin protein or its variant;

grafting the virus-treated blood vessel in said mammal, wherein said thrombomodulin protein or its variant is expressed in said virus-treated blood vessel in a amount sufficient to reduce re-occlusion or intimal hyperplasia in the grafted blood vessel.

2. The method of Claim 1, wherein said thrombomodulin protein has the amino acid sequence of SEQ ID NO:2.

3. The method of Claim 1, wherein said gutless adenoviral vector further comprises a regulatory element operably linked to the DNA sequence.

4. The method of Claim 3, wherein the regulatory element is a constitutive promoter selected from a group consisting of CMV promoter and RSV promoter.

5. The method of Claim 1, wherein the expression of said polynucleotide encoding a thrombomodulin protein or its variant is under the control of an inducible system.

6. The method of Claim 1, wherein said gutless adenoviral vector is produced using a shuttle vector comprising a pBR322 replication origin, a selectable marker gene, an adenovirus left inverted terminal repeat, an adenovirus encapsidation signal, an intronic sequence, and an adenovirus left inverted terminal repeat.

7. The method of Claim 6, wherein said selectable marker gene is Kanamycin resistance gene.

8. The method of Claim 1, wherein said mammal is human

9. The method of Claim 1, wherein said infecting step further comprises:

5 filling the blood vessel with a complete viral delivery system comprising of
1: 1 mixture of Ham's F12 medium and DMEM, an effective amount of the gutless
adenovirus vector, and an acellular oxygen carrier; and

 incubating the blood vessel with the complete viral delivery system for a
desired period of time.

10 10. The method of claim 9, wherein said acellular oxygen carrier is selected
from the group consisting of unmodified hemoglobin, chemically modified
hemoglobin and perfluorochemical emulsions.

 11. The method of claim 10, wherein said unmodified hemoglobin or
chemically modified hemoglobin is used in the range of 3 g/dl to 10 g/dl.

15 12. The method of claim 9, wherein the complete viral delivery system
further comprises at least one of L-glutamine, sodium bicarbonate, or antibiotic-
antimycotic.

 13. The method of claim 9, wherein the desired period of time is between
10 to 45 minutes.

20 14. A method for treating a vascular disease in a mammal, wherein said
method comprising the steps of:

 evacuating a clot from a blood vessel in said mammal;

 isolating a segment of the blood vessel around the evacuation site; and

 infecting the segment of blood vessel *in vivo* using a gutless adenoviral

vector comprising a polynucleotide encoding a thrombomodulin protein or its variant;

wherein the thrombomodulin protein or its variant is expressed in a amount sufficient to reduce re-occlusion or intimal hyperplasia in the infected segment of the blood vessel.

15. The method of claim 14, wherein the isolating step further comprises the steps of:

inserting a balloon catheter to the site of evacuation; and

inflating a proximal balloon and a distal balloons to isolate the vessel

segment around the site of evacuation.

16. The method of claim 14, wherein said infecting step further comprises the steps of:

filling the isolated vessel segment with a complete viral delivery system comprising of 1: 1 mixture of Ham's F12 medium and DMEM, an effective amount of the gutless adenovirus vector, and an acellular oxygen carrier; and

incubating the isolated vessel segment with the complete viral delivery system for a desired period of time.

17. The method of Claim 14, wherein said thrombomodulin protein has an amino acid sequence of SEQ ID NO:2.

18. The method of Claim 14, wherein said gutless adenoviral vector comprises a regulatory element operably linked to a DNA sequence encoding a thrombomodulin protein or a variant of the thrombomodulin protein.

19. The method of Claim 18, wherein said regulatory element is a constitutive promoter selected from a group consisting of CMV promoter and RSV promoter.

20. The method of Claim 14, wherein said polynucleotide encoding a thrombomodulin protein or its variant is under the control of an inducible system.

21. The method of Claim 14, wherein said gutless adenoviral vector is produced using a shuttle vector comprising a pBR322 replication origin, a selectable marker gene, an adenovirus left inverted terminal repeat, an adenovirus encapsidation signal, an intronic sequence, and an adenovirus left inverted terminal repeat.

22. The method of Claim 14, wherein said mammal is human.

23. A method for treating a vascular disease in a mammal comprising administering a therapeutically effective amount of a gutless adenovirus vector into a segment of a blood vessel using a stent, wherein said gutless adenovirus vector is capable of expressing a thrombomodulin protein or a variant of the thrombomodulin protein.

24. The method of Claim 23, wherein said thrombomodulin protein has an amino acid sequence of SEQ ID NO:2.

25. The method of Claim 23, wherein said gutless adenovirus vector is embedded in said stent and is released only at a treatment site.

26. A composition for treating a vascular disease, comprising:
a gutless adenovirus capable of expressing thrombomodulin protein or a variant of the thrombomodulin protein, said gutless adenovirus is produced using a shuttle vector comprising a pBR322 replication origin, a selectable marker gene, an

adenovirus left inverted terminal repeat, an adenovirus encapsidation signal, an intronic sequence, and an adenovirus right inverted terminal repeat.

27. A pharmaceutical composition for treating a vascular disease according to Claim 26, further comprising a pharmaceutically acceptable carrier.